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Tosvinyl and Besvinyl as Protecting Groups of Imides, Azinones, Nucleosides, Sultams, and Lactams. Catalytic Conjugate Additions to Tosylacetylene

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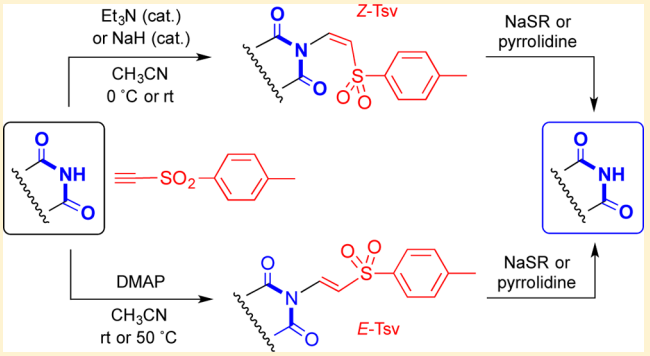
Supporting Information

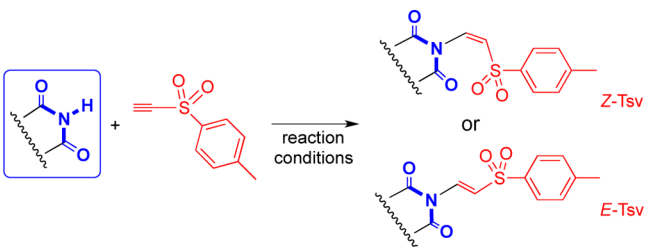
ABSTRACT: The use of the 2-(4-methylphenylsulfonyl)-ethenyl (tosvinyl, Tsv) group for the protection of the NH group of a series of imides, azinones (including AZT), inosines, and cyclic sulfonamides has been examined. The Tsv-protected derivatives are obtained in excellent yields by conjugate addition to tosylacetylene (ethynyl *p*-tolyl sulfone). The stereochemistry of the double bond can be controlled at will: with only 1 mol % of Et_3N or with catalytic amounts of NaH, the *Z* stereoisomers are generated almost exclusively, while the *E* isomers are obtained using a stoichiometric amount of DMAP. Analogous phenylsulfonylvinyl-protected groups (with the besvinyl or Bsv group instead of Tsv) are obtained stereospecifically by reaction with (*Z*)- or (*E*)-bis(phenylsulfonyl)ethene. For lactams and oxazolidinones, this last method is much better. The Tsv and Bsv groups are stable in the presence of non-nucleophilic bases and to acids. They can be removed highly effectively via a conjugate addition−elimination mechanism using pyrrolidine or sodium dodecanethiolate as nucleophiles.



INTRODUCTION

Due to the strong electron-withdrawing character of the sulfonyl group, 1-alkynyl and 1-alkenyl sulfones can participate as acceptors in Michael-type additions and in [4 + 2]-, [3 + 2]-, and [2 + 2]-cycloadditions. Consequently, they have many synthetic applications.[1] We were interested in the conjugate additions of nucleophiles to ethynyl sulfones, in comparison with those to other electron-deficient triple bonds.[2] In this regard, we planned to take advantage of the reactivity of commercially available 1-(ethynylsulfonyl)-4-methylbenzene (ethynyl *p*-tolyl sulfone, Ts−C≡CH), commonly called tosylacetylene, to develop a procedure for the protection of heterocyclic compounds with activated NH groups. As shown in Scheme 1, this would require a conjugate addition (aza-Michael addition) under very mild conditions to afford quickly, quantitatively, and selectively either *Z*-vinyl or *E*-vinyl sulfone derivatives as desired. The stability of these 2-(4-tolylsulfonyl)-ethenyl groups (2-tosylvinyl, tosvinyl, Tsv),[3] and appropriate conditions for their removal should be then evaluated.

Scheme 1. Tosylacetylene as a Reagent for the Protection of CONHCO and Related Groups



The reaction of tosylacetylene with thiols was examined exhaustively by the research group of Plumet and Arjona,[4] with whom some of us collaborated to develop a chemoselective protection scheme for thiol groups.[4b,5] O-Nucleophiles and amines also react with tosylacetylene,[1c] and there are also a few examples of the addition of the CONH groups of heterocyclic compounds to alkynyl sulfones.[6] However, despite the scarcity of good methods for the protection of these moieties,[3] and even though it is a functionality that very often requires protection during the synthesis of drugs, the use of the Tsv group has not been studied in detail.[6b,7] In this connection, we have comparatively evaluated, for the first time, the protection with Tsv of several relatively acidic NH groups (see Figure 1): carboximides **1a** and **1b**; the special imide moiety of a pyrimidine nucleoside (*O*-Ac-AZT, **1c**); the particular amide groups of 2-pyridone (**1d**), 2-hydroxyquinazoline (quinazolone **1e**), and inosine **1f**; cyclic sulfonamides (sultams **1g** and **1h**); an *N*-acylsultam (saccharin, **1i**). Less acidic NH-containing substrates such as lactams **1j** and **1k** and a cyclic carbamate (oxazolidinone **1l**, Figure 1) were also included in the set. It was crucial that Tsv could be introduced with *Z* or *E*

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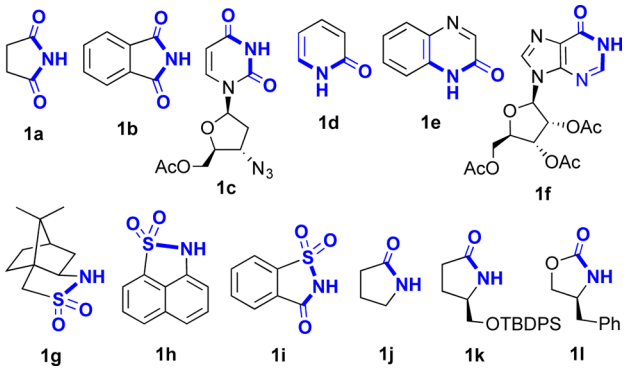


Figure 1. Set of compounds studied.

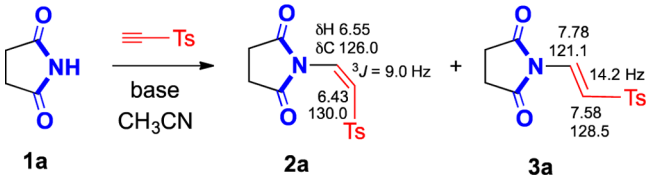
configuration as desired, to avoid the formation of mixtures of stereoisomers that would complicate the characterization of the protected products. In several cases, the preparation of derivatives with a 2-(benzenesulfonyl)ethenyl or 2-besylvinyl substructure ($PhSO_2CH{=}CH$, besvinyl, Bsv) was also studied for the sake of comparison. We believe that this study expands the scope of the use of Tsv and related groups in organic synthesis, which is currently somewhat limited.

RESULTS AND DISCUSSION

The great reactivity of electron-deficient triple bonds, linked to strong EWGs such as SO_2Ar, with nucleophiles should facilitate the attachment of Tsv to the nitrogen of amides and imides, which are poorly nucleophilic unless they are converted into their more reactive anions. Several bases and catalysts are reported for similar reactions.[2,4,6] To identify the best conditions for the stereoselective introduction of Tsv, we started by studying the reaction of succinimide (**1a**), with a relatively acidic NH group, with tosylacetylene, promoted by Et_3N, DIPEA (a basic but poorly nucleophilic tertiary amine), NaH, DMAP, and DABCO (the last two less basic than a standard tertiary amine but highly nucleophilic). The results of this preliminary screening are shown in Table 1.

Succinimide, **1a**, does not react with tosylacetylene alone at rt (entry 1), as expected, but the reaction is strongly accelerated by the presence of a small amount of a base. All the basic catalysts tested afford complete conversion in less than 30 min, even at 0 °C and with only a trace of the base. The *Z* stereoisomer **2a** is always the major product, although the degree of selectivity changes depending on the base and conditions. The results obtained using Et_3N or DIPEA are similar although the reactions with the latter (compare entry 5 to 2) are slightly more *Z*-selective. To obtain **2a** exclusively, with Et_3N, it is necessary to work with only a trace of the base at 0 °C (entry 4). Catalytic amounts of NaH (entries 8 and 9) also afford **2a** with complete stereoselectivity, instantaneously. Finally, we examined two bases of well-known nucleophilicity, DMAP and DABCO,[8] which gave mixtures of stereoisomers (entries 10−12 and 14). However, on prolonged heating with DMAP or DABCO the more stable *E* isomer (**3a**) became the major compound (entries 13 and 15); the yields obtained with DABCO were slightly lower than with DMAP.[9] Heating in the presence of Et_3N caused a much slower isomerization. Thus, it appears that adducts generated under kinetic control (basic medium)[5] isomerize to the thermodynamically favored *E* isomers in the presence of the more nucleophilic bases (slowly at rt, quantitatively after prolonged heating).

Table 1. Screening of the Reaction Conditions for the Addition of Succinimide (1a) to Tosylacetylene[a]

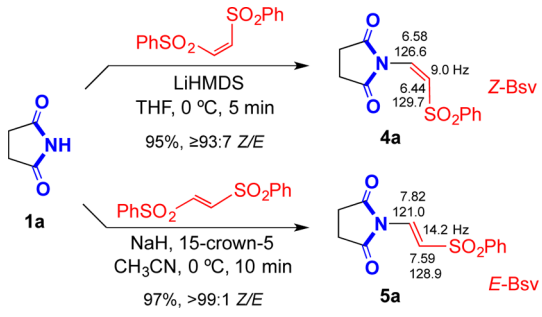


entry	base or catalyst (equiv)	*T* (°C)	time (h)	conv (%)	yield (%)	**2a**/**3a** (*Z*/*E*)[b]
1		20	24	0		
2	Et_3N (0.1)	20	0.2	100	87	86:14
3	Et_3N (0.1)	0	0.2	100	91	88:12
4	Et_3N (0.01)	0	0.2	100	92	>99:1[c]
5	DIPEA (0.1)	20	0.2	100	95	>99:1[c]
6	DIPEA (0.05)	20	0.2	100	94	>99:1[c]
7	DIPEA (0.01)	0	0.3	100	92	>99:1[c]
8	NaH (0.2)	20	<0.2	100	97	>99:1[c]
9	NaH (0.05)	20	<0.2	100	97	>99:1[c]
10	DMAP (0.1)	20	0.5	100	92	93:7
11	DMAP (0.5)	20	0.2	100	92	74:26
12	DMAP (1.0)	20	0.2	100	90	55:45
13	DMAP (1.0)	50	48	100	90	<1:99[c]
14	DABCO (0.2)	20	0.2	100	88	70:30
15	DABCO (1.0)	50	48	100	84	<1:99[c]

[a]Standard conditions: **1a** and tosylacetylene (1.2 equiv) were dissolved in CH_3CN (0.1 M) under N_2, and the base was added at 0 °C; stirring was maintained at the temperature shown above, for the time indicated. The isolated yields of isomers *E*+*Z* are given. [b]*E*/*Z* ratios were determined by ^1H NMR (400 MHz). [c]The minor isomer was not detected by ^1H NMR (400 MHz).

The NMR signals of the products proved to be diagnostic. This is an advantage of this kind of protecting group (with a double bond), as the introduction and removal can be easily followed by NMR spectroscopy. For the sake of comparison we allowed **1a** to react with (*Z*)-1,2-bis(phenylsulfonyl)ethene and with (*E*)-1,2-bis(phenylsulfonyl)ethene, both commercially available.[10] As summarized in Scheme 2, adduct *Z* (**4a**) was

Scheme 2. Reaction of 1a with 1,2-Bis(sulfonyl)ethenes



formed with the former reagent and adduct *E* (**5a**) with the latter, with an excellent stereospecificity.[10] By analogy to the Tsv group,[3] we call these 2-(phenylsulfonyl)ethenyl substituents (*Z*)- and (*E*)-besvinyl groups, or simply *Z*-Bsv and *E*-Bsv, as they contain benzenesulfonylvinyl moieties. The NMR spectra of **4a** and **5a** correlated perfectly with those of **2a** and **3a**, respectively, as anticipated.[11]

Having established suitable conditions for the selective preparation of either the *Z*- or *E*-protected succinimides, we

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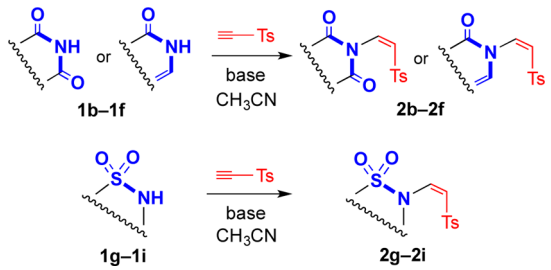
extended the study to other compounds containing similar, relatively acidic NH, such as compounds **1b–i** shown in Figure 1. The results obtained in the preparation of *Z* derivatives, **2**, are shown in Table 2. In all cases, the yields were excellent.

Table 2. Preparation of *Z*-Tsv-Protected Compounds 2b–i[a]



entry	substrate	base (equiv)	*T* (°C)	time (h)	yield (%)	**2**/**3** (*Z*/*E*)[b]
1	**1b**	Et_3N (0.01)	0	0.2	89	>99:1[c]
2	**1c**	Et_3N (0.03)	0	0.3	85	>99:1[c]
3	**1d**	Et_3N (0.01)	0	0.6	92	98:2
4	**1d**	DIPEA (0.01)	0	1.0	89	93:7
5	**1e**	Et_3N (0.01)	20	0.1	92	>99:1[c]
6	**1e**	NaH (0.2)	20	0.5	87	>99:1[c]
7	**1f**[d]	Et_3N (0.03)	10	0.5	86	95:5
8	**1g**	Et_3N (0.03)	−5	1.0	87	>99:1[c]
9	**1h**	Et_3N (0.03)	20	2.5	96	98:2
10	**1i**	NaH (0.2)	20	1.6	90[e]	>99:1[c]

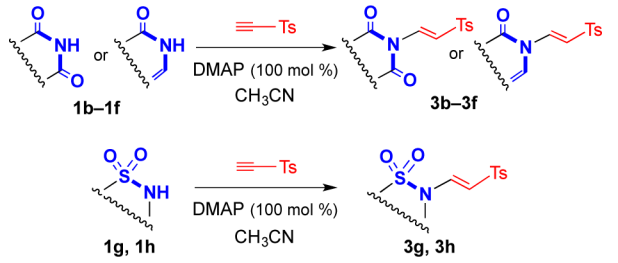
[a]Standard conditions: **1b–i** and tosylacetylene (1.2 equiv) were dissolved in CH_3CN (0.1 M) under N_2, and the corresponding base was slowly added at 0 °C. Stirring at the temperature shown in the table was maintained for the time indicated. The isolated yields of isomers *E*+Z are given. [b]*E*/*Z* ratios were determined by ^1H NMR. [c]The minor isomer was not detected by ^1H NMR. [d]CH_3CN/CH_2Cl_2 (1:1) was used as the solvent. [e]Conversion was complete, but the product partially decomposed when purification was attempted by column chromatography.

Experiments carried out in 1:1 CH_2Cl_2/CH_3CN or in THF, although not included in Table 2 for the sake of simplicity, gave similar or only slightly lower results, respectively. The *E* isomers were rarely detected; they were only noted in the cases of pyridone (**1d**), inosine (**1f**), and naphthosultam (**1h**), but as very minor products. Saccharin (**1i**), with a highly acidic NH (pK_a = 1.6 in H_2O,[12a] pK_a = 4 in DMSO[12b]), with a poorly nucleophilic anion, reacts very slowly, even in the presence of stoichiometric amounts of DIPEA or Et_3N; however, *Z*-Tsv-protected saccharin **2i** can be prepared by using NaH (entry 10). It is uncommon for an *N*-acylsulfonamide moiety embedded in a drug to require protection, but we included this compound in the set to check the capacity of "sodium saccharine" to behave as a nucleophile against triple bonds activated by an electron-withdrawing group.[13]

Isomerization of *Z* isomers, once isolated, to *E* isomers could be accomplished by nucleophilic catalysis. For example, isomerization of (*Z*)-**2b** to (*E*)-**3b** was complete by addition of a stoichiometric amount of DMAP and heating at 50 °C for 48 h. With substoichiometric amounts of DMAP or DABCO, the isomerization was incomplete.[14]

We could obtain directly the *E* stereoisomers as indicated in the case of **1a**, that is, by reaction of the substrate with 100 mol % of DMAP for many hours (Table 3). In fact, to achieve complete formation of the *E* isomer, heating was necessary in most of the cases, but not always (entries 3 and 5). With 1

Table 3. Preparation of *E*-Tsv-Protected Compounds 3b–h[a]



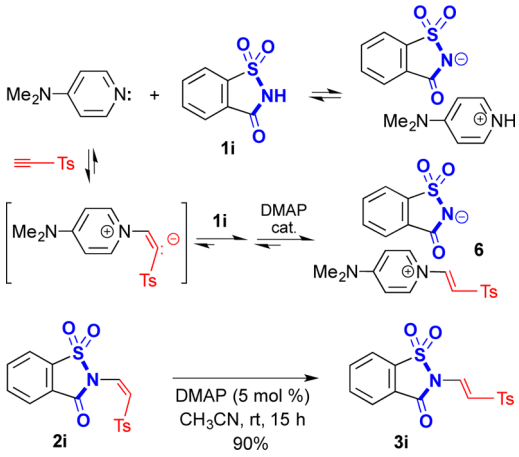
entry	substrate	base	*T* (°C)	time (h)	yield (%)	**3**, *E*/*Z*[b]
1	**1b**	DMAP	50	48	98	**3b**, >99:1
2	**1c**	DMAP	50	48	80	**3c**, >99:1
3	**1d**	DMAP	20	24	96	**3d**, >99:1
4	**1e**	DMAP	50	48	84	**3e**, >99:1
5	**1f**[c]	DMAP	20	48	90	**3f**, >99:1
6	**1g**	DMAP	50	48	82	**3g**, >99:1
7	**1h**	DMAP	50	48	97	**3h**, >99:1

[a]Standard conditions: **1a–h** and tosylacetylene (1.2 equiv) were dissolved in CH_3CN (0.1 M) under N_2, and DMAP (1.0 equiv) was then added. Stirring at the temperatures shown in the table was maintained for the time indicated. [b]*E*/*Z* ratios determined by ^1H NMR. [c]CH_3CN/CH_2Cl_2 (1:1) was used as the solvent.

equiv of DABCO instead of 1 equiv of DMAP, the yields of **3** were lower (in the 60–88% range, data not shown in Table 3).[9]

Again, the behavior of saccharin was special. Mixing equivalent amounts of saccharin (**1i**) and DMAP in CH_3CN caused immediate precipitation of the 4-(dimethylamino)-pyridinium salt of saccharin, which dissolved as soon as tosylacetylene was added. After a few minutes another salt precipitated, which was identified as **6**.[15] This probably results from conjugate addition of DMAP to tosylacetylene followed by protonation of the resulting anion by saccharin (Scheme 3).

Scheme 3. Formation of Salt 6 and Isomerization of 2i to 3i



The isolation of this salt is consistent with the role of DMAP as a nucleophilic catalyst or promoter. Compound **6** remained unaltered when heated in CH_3CN for 1 day. Nevertheless, **3i** was isolated in 90% yield by treatment of its *Z* stereoisomer, **2i**, prepared as reported in Table 2, with a catalytic amount of DMAP at rt.

The less acidic lactams **1j** and **1k** and oxazolidinone **1l** do not react with H–C≡C–Ts under the conditions optimized for the *Z*-Tsv and *E*-Tsv derivatives.[16] As an alternative, we

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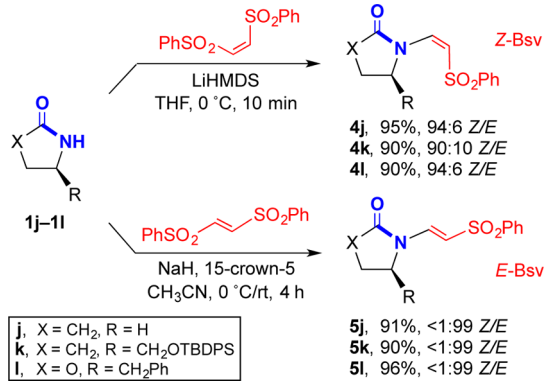
could examine their synthetic equivalents X−CH═CH−SO_2Ar (X = halogen or other good leaving groups).[17] In practice, we have used 1,2-bis(phenylsulfonyl)ethenes ($PhSO_2$−CH═CH−SO_2Ph) for the protection of **1j−l** (as Bsv derivatives, see Scheme 2), by means of the known stereospecific Ad−E reaction[6b,7,10] of nucleophiles to these activated alkenes. Our results are summarized in Scheme 4. Thus, by reaction with

Scheme 4. Preparation of 4j−l and 5j−l

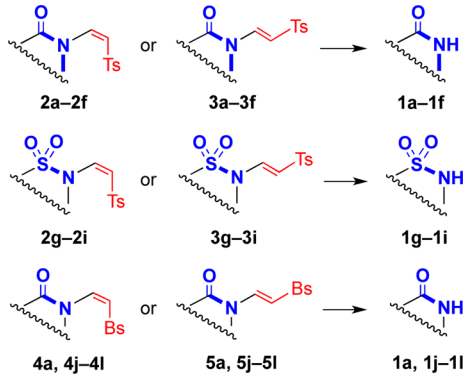


(*Z*)-1,2-bis(phenylsulfonyl)ethene, the lithium salts of **1j−l** afforded *Z*-Bsv-protected compounds **4j−l** with high selectivity, whereas with the sodium salts (generated from NaH or NaHMDS, either in substoichiometric or stoichiometric amounts) we obtained a mixture of *Z*-Bsv and *E*-Bsv derivatives. On the other hand, by reaction with (*E*)-1,2-bis(phenylsulfonyl)ethene, the sodium salts of **1j−l**, in the presence of an excess of 15-crown-5, gave exclusively the desired *E*-Bsv derivatives.

The stabilities of the CON−Tsv, CON−Bsv, SO_2N−Tsv, and SO_2N−Bsv bonds were examined in basic and acidic media. (1) Removal of the TBDPS group of **4k** was accomplished with TBAF at rt in excellent yield with partial *Z* to *E* isomerization of the Bsv group; meanwhile, use of TBAF buffered with HOAc cleaved the silyl ether while hardly affecting the Tsv group (no isomerization). (2) Compound **5k** could be α-benzylated in good yield (LiHMDS, THF, −78 °C, benzyl bromide, rt), the Bsv group remaining intact. (3) The acetyl group of **2c** could be removed quantitatively by treatment with 1% NaOMe in MeOH, while the *Z* configuration of the Tsv group was maintained; however, these reaction conditions could not be applied to **2f**, which suffered secondary reactions. (4) When treated with 10% TsOH·H_2O in MeOH at rt, the acetyl groups of inosine **3f** were slowly cleaved but the Tsv group remained unaltered; also, compounds **2b**, **2g**, and **5l** were recovered intact after treatment with these reagents even on heating at 55 °C for 48 h. From these experiments, we can conclude that the Tsv group is not sensitive to acid media or to non-nucleophilic bases.

Several deprotection procedures, based on an addition−elimination mechanism, were examined. A selection of the most relevant results is shown in Table 4. The most general method was the use of dodecanethiol and an excess of sodium hydride (method A). The deprotected compounds were isolated in excellent yields, as well as coproducts $CH_3(CH_2)_{11}$SCH═CHTs or $CH_3(CH_2)_{11}$SCH═CHBs (only isomers *E*, $^3J_{HH}$ = 14.6 Hz). The excess of NaH (relative to the thiol) was necessary, otherwise the initial intermediates from conjugate addition of the nucleophile (*N*,*S*-acetals, thiohemiaminals)[18]

Table 4. Removal of the Tsv and Bsv Groups with Nucleophiles



entry	substrate	method[a]	*T* (°C)	time (h)	**1a−i** yield[b] (%)
1	**2a**	A	50	0.25	98
2	**2a**	A	20	15	97
3	**3a**	A	20	15	82
4	**4a**	A	20	15	90
5	**5a**	A	20	15	92
6	**2b**	A	20	0.25	95
7	**3b**	A	20	0.25	82
8	**2c**	A	20	0.5	97
9	**2c**	C	20	2	96
10	**3c**	C	20	2	97
11	**2d**	A	20	0.5	97
12	**2d**	C	20	0.5	95
13	**3d**	C	20	0.5	90
14	**2e**	A	20	0.5	85
15	**2e**	C	20	1	75
16	**3e**	C	20	1	91
17	**2f**	B	0	0.5	91
18	**3f**	A	0	0.5	90
19	**2g**	A	20	2	70
20	**2g**	C[c]	55	48	91[d]
21	**3g**	C[c]	55	48	86[e]
22	**2h**	A[f]	20	2	95
23	**2h**	C[c]	20	2	88
24	**2i**	B	20	0.5	89
25	**2i**	C[c]	20	0.5	70
26	**3i**	C[c]	20	1	90
27	**4j**	D	55	5.5	81
28	**5j**	D	55	5.5	77
29	**4k**	D	55	24	70
30	**5k**	D	55	20	76[e]
31	**4l**	C[c]	20	18	88[e]
32	**5l**	C[c]	55	4.5	94

[a]Method A: dodecanethiol (1.5 equiv), NaH (3.0 equiv), CH_3CN. Method B: sodium dodecanethiolate (1.2 equiv), CH_3CN. Method C: pyrrolidine (2.0 equiv), CH_3CN. Method D: pyrrolidine (4.0 equiv), NaH (0.3 equiv), CH_3CN. [b]Isolated yields after removal of reagent excess and separation from Nu−CH═CH−EWG by flash column chromatography. Conversions were complete. [c]With 4.0 equiv of pyrrolidine. [d]Brsm yields (92% conversion). [e]Brsm yields (90% conversion). [f]THF as the solvent instead of CH_3CN.

predominated. Nevertheless, sodium dodecanethiolate alone, without additional NaH (method B), was enough in some cases (Table 4, entries 17 and 24). Lactams **4j** and **4k** and oxazolidinone **4l** isomerized to the corresponding *E* isomers **5j−l** and did not react further when treated with sodium dodecanethiolate (by method A or B); this result was not

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unexpected, bearing in mind that the dodecanethiolate ion might be a better leaving group than the anions of **1j**−**l**.

We also explored the performance of pyrrolidine (method C) in this transformation, with satisfactory results, except for some particular cases, viz., we noted that pyrrolidine attacked the carbonyl carbon of Tsv-protected imides **2a**, **2b**, **3a**, **3b**, and **3f** rather than undergoing the desired conjugate addition. The deprotection of camphorsultam derivatives **2g** and **3g** was very slow, due to steric hindrance, but camphorsultam could be isolated in good yield by increasing the amount of pyrrolidine and the temperature (see entries 20 and 21). Lactams **4j**, **4k**, **5j**, and **5k** could be deprotected in good yields by the combined use of pyrrolidine (4.0 equiv) and NaH (0.3 equiv) (method D, entries 27−30); in all other cases, stable aminal intermediates predominated and could be isolated.[19] Geometrical isomers **4l** and **5l** show a remarkable difference in reactivity when treated with pyrrolidine (entries 31 and 32). Whereas **4l** (*Z* isomer) reacted smoothly at rt and furnished **1l** in excellent yield, its *E* isomer **5l** did not react. Only after heating the reaction mixture to 55 °C did we achieve complete conversion of **5l** to **1l**. In general, we observed that *Z*-Tsv and *Z*-Bsv were removed more readily than their thermodynamically more stable *E* isomers, as was to be expected.

The *N*-Tsv- and *N*-Bsv-protected compounds may be transformed to the corresponding *N*-vinyl derivatives, via cleavage of the C−SO_2 bonds under reductive conditions.[20] Also, the Tsv- and Bsv-containing compounds can be hydrogenated (H_2 balloon, Pd/C) within minutes to give quantitatively the corresponding 2-tosylethyl (tosethyl, Tse[6b]) and 2-(benzenesulfonyl)ethyl (besethyl, Bse) derivatives, as we checked with compounds **3a**, **3e**, and **5l**.

CONCLUSIONS

A series of heterocyclic compounds containing CONHCO, CONHCH═CH, CONHCH═N, and SO_2NH moieties react with tosylacetylene to furnish *N*-2-tosylethenyl adducts (tosvinyl or Tsv derivatives) with *Z* configuration in the presence of Et_3N or NaH as catalysts. Isomeric *E* adducts can be produced by using DMAP in stoichiometric amounts. Thus, the *Z*-Tsv or *E*-Tsv protecting groups can be introduced at will. Analogous derivatives and analogous protected lactams and oxazolidinones, with 2-(benzenesulfonyl)ethenyl substituents (called here *Z*-besvinyl or *Z*-Bsv, and *E*-besvinyl or *E*-Bsv), can also be stereoselectively obtained by reaction with *Z*- or *E*-1,2-bis(phenylsulfonyl)ethene, respectively. The Tsv and Bsv groups are stable in acid media and non-nucleophilic bases and can be removed efficiently via an addition−elimination mechanism by treatment with good nucleophiles such as sodium dodecanethiolate or pyrrolidine, depending on the case.

EXPERIMENTAL SECTION

General Information. Unless specified otherwise, all starting materials and reagents were obtained from commercial suppliers and used without further purification. All reactions were conducted in oven-dried glassware, under dry nitrogen, with anhydrous solvents, which were dried and distilled before use according to standard procedures. Solvents used for isolation of products and chromatography were glass distilled. Analytical thin-layer chromatography (TLC) was performed on 0.25 mm silica gel plates (F_{254}); retention factors (R_f) are approximate. Flash column chromatography was performed on silica gel 60 (35−70 μm). Yields were determined after purification of the desired compound by column chromatography on silica gel. Melting points are uncorrected. ^{1}H NMR spectra were recorded on 400 MHz spectrometers. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$ impurity in $CDCl_3$, δ 7.26 ppm; CD_3SOCHD_2 in DMSO-d_6, δ 2.50 ppm). Data are reported in the following order: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants in hertz, integration; the aromatic protons of Ts groups (AA′XX′ systems) usually appear as doublets (br d in the expanded spectra). ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO on the above-mentioned spectrometers (100.6 MHz for ^{13}C) with complete proton decoupling. Chemical shifts are reported in ppm with the solvent as the internal standard ($CDCl_3$, δ 77.2 ppm; DMSO-d_6, δ 39.5 ppm). Where necessary, 2D NMR experiments (HSQC and NOESY) were carried out to assist in structure elucidation and signal assignments. All the IR spectra were recorded on a FT-IR instrument equipped with an ATR accessory; only the relevant bands are reported, in cm^{-1}. All the high-resolution mass spectra (HRMS) were obtained by the electrospray ionization (ESI+, TOF) technique.

General Procedure for the Addition of Imides, Azinones, Nucleosides, and Sultams to Tosylacetylene, To Obtain 2. Et_3N (as a 0.1 M solution in CH_3CN) or NaH was slowly added at 0 °C to a solution of the corresponding substrate and tosylacetylene (ethynyl 4-methylphenyl sulfone, 1.2 equiv) under a N_2 atmosphere. The reaction was stirred at the temperature indicated in Table 1 (entries 2−9) and Table 2 until TLC analysis indicated complete consumption of the substrate. The solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2, washed with 0.5 M HCl and brine, dried over anhyd $MgSO_4$, filtered, and concentrated. Purification by flash column chromatography on silica gel afforded stereopure alkenes **2**.

*Compound **2a** (>99:1 Z/E, 78 mg, 92%, with 0.01 equiv of Et_3N), N-[(Z)-2-(4-methylphenylsulfonyl)ethenyl]succinimide.* White solid; mp 171−172 °C; R_f = 0.34 (hexanes/EtOAc, 20:80); ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 2.88 (s, 4H), 6.43 (d, *J* = 9.0, 1H), 6.55 (d, *J* = 9.0, 1H), 7.36 (d, *J* = 8.4, 2H), 7.82 (d, *J* = 8.4, 2H); ^{13}C NMR ($CDCl_3$) δ 21.8, 28.9, 126.2, 128.3, 130.0, 130.1, 136.9, 145.4, 174.5; IR 1780, 1714, 1613; HRMS *m*/*z* calcd for $C_{13}H_{14}NO_4S^+$ $[M + H]^+$ 280.0638, found 280.0632.

__2b__ (>99:1 Z/E, 110 mg, 89%, with 0.01 equiv of Et_3N), N-[(Z)-2-(4-methylphenylsulfonyl)ethenyl]phthalimide. White solid; mp 173−175 °C; R_f = 0.55 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.43 (s, 3H), 6.42 (d, *J* = 9.2, 1H), 6.76 (d, *J* = 9.2, 1H), 7.35 (d, *J* = 8.2, 2H), 7.80 (m, AA′ subsystem, 2H), 7.86 (d, *J* = 8.2, 2H), 7.96 (m, BB′, 2H); ^{13}C NMR ($CDCl_3$) δ 21.8, 124.4, 124.9, 127.9, 128.3, 130.0, 132.1, 134.9, 137.5, 145.1, 165.4; IR 1786, 1721, 1590; HRMS *m*/*z* calcd for $C_{17}H_{14}NO_4S^+$ $[M + H]^+$ 328.0638, found 328.0634.

__2c__ (>99:1 Z/E, 81 mg, 85%, with 0.03 equiv of Et_3N), 5′-O-acetyl-3′-azido-3′-deoxy-3-[(Z)-2-(4-methylphenylsulfonyl)-ethenyl]-thymidine. Foam; R_f = 0.12 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$) δ 1.97 (br d, *J* = 1.2, 3H), 2.13 (s, 3H), 2.43 (s, 3H), 2.44−2.61 (m, 2H), 4.11 (dt, *J* = 5.5, *J* = 4.0, 1H), 4.21 (dt, *J* = 7.3, *J* = 6.0, 1H), 4.35 (dd, *J* = 12.3, *J* = 3.7, 1H), 4.39 (dd, *J* = 12.3, *J* = 4.4, 1H), 6.09 (t, *J* = 6.0, 1H), 6.48 (d, *J* = 8.8, 1H), 6.71 (d, *J* = 8.8, 1H), 7.32 (q, *J* = 1.2, 1H), 7.33 (d, *J* = 8.2, 2H), 7.78 (d, *J* = 8.2, 2H); ^{13}C NMR ($CDCl_3$) δ 12.7, 20.5, 21.3, 37.3, 60.2, 63.1, 81.7, 86.3, 109.5, 127.7, 129.6, 130.4, 134.6, 136.4, 144.8, 148.8, 161.9, 170.0; IR 2103, 1739, 1715, 1662; HRMS *m*/*z* calcd for $C_{21}H_{24}N_5O_7S^+$ $[M + H]^+$ 490.1391, found 490.1387.

__2d__ (98:2 Z/E, 64 mg, 92%, with 0.01 equiv of Et_3N). Data for chromatographically pure N-[(Z)-2-(4-methylphenyl-sulfonyl)-ethenyl]-2-pyridone. White solid; mp 110−112 °C; R_f = 0.40 (CH_2Cl_2/MeOH, 98:2); ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3H), 6.24 (td *J* = 6.8, 1.2, 1H), 6.34 (d, *J* = 9.5, 1H), 6.47 (br d, *J* = 9.4, 1H), 7.30 (d, *J* = 8.2, 2H), 7.33−7.39 (m, 1H), 7.35 (d, *J* = 9.5, 1H), 7.71−7.76 (m, 1H), 7.73 (d, *J* = 8.2, 2H); ^{13}C NMR ($CDCl_3$) δ 21.8, 105.8, 120.8, 125.7, 127.8, 130.1, 135.4, 136.9, 138.4, 141.5, 145.5, 161.6; IR 1671, 1619; HRMS *m*/*z* calcd for $C_{14}H_{14}NO_3S^+$ $[M + H]^+$ 276.0689, found 276.0690.

__2e__ (>99:1 Z/E, 163 mg, 92%, with 0.01 equiv of Et_3N), 1-[(Z)-2-(4-methylphenylsulfonyl)ethenyl]-2-quinoxalinone. White solid; mp 170−172 °C; R_f = 0.58 (CH_2Cl_2/EtOAc, 1:1); ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H), 6.79 (d, *J* = 8.8, 1H), 6.89 (d, *J* = 8.8, 1H), 7.19 (dd, *J* =

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8.4, J = 1.1, 1H), 7.23 (d, J = 8.2, 2H), 7.39 (ddd, J = 8.0, J = 7.5, J = 1.1, 1H), 7.55 (ddd, J = 8.4, J = 7.5, J = 1.5, 1H), 7.65 (d, J = 8.2, 2H), 7.87 (dd, J = 8.0, J = 1.5, 1H), 8.18 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 114.9, 124.8, 128.5, 129.1, 129.9, 130.6, 131.3, 131.9, 133.0, 135.3, 135.7, 145.8, 149.9, 153.3; IR 1678, 1607; HRMS m/z calcd for $C_{17}H_{15}N_2O_3S^+$ $[M + H]^+$ 327.0798, found 327.0800.

2f *(95:5 Z/E, 50 mg, 86%, with 0.03 equiv of Et_3N). Data for chromatographically pure 2′,3′,5′-tri-O-acetyl-1-[(Z)-2-(4-methylphenylsulfonyl)ethenyl]inosine.* White solid; mp 96−98 °C; R_f = 0.45 (CH_2Cl_2/MeOH, 95:5); ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 3H), 2.16 (s, 6H), 2.39 (s, 3H), 4.36−4.49 (m, 3H), 5.57 (t, J = 5.0, 1H), 5.81 (t, J = 5.4, 1H), 6.16 (d, J = 5.4, 1H), 6.56 (d, J = 9.2, 1H), 7.29 (d, J = 8.2, 2H), 7.36 (d, J = 9.2, 1H), 7.72 (d, J = 8.2, 2H), 7.96 (s, 1H), 8.31 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.6, 20.9, 21.8, 63.1, 70.6, 73.5, 80.6, 86.8, 122.7, 125.2, 127.9, 130.2, 135.0, 137.2, 139.4, 145.2, 145.3, 146.1, 155.1, 169.4, 169.7, 170.4; IR 1742, 1704, 1631; HRMS m/z calcd for $C_{25}H_{27}N_4O_{10}S^+$ $[M + H]^+$ 575.1442, found 575.1447.

2g *(>99:1 Z/E, 64 mg, 87%, with 0.03 equiv of Et_3N), (S)-N-[(Z)-2-(4-methylphenylsulfonyl)ethenyl]-2,10-camphorsultam.* White solid; mp 131−133 °C; R_f = 0.54 (CH_2Cl_2/MeOH, 99.5:0.5); ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 3H), 0.94 (s, 3H), 1.41−1.46 (m, 1H), 1.53−1.59 (m, 1H), 1.90−1.97 (m, 3H), 2.25 (dd, J = 13.7, J = 8.0, 1H), 2.36−2.42 (m, 1H), 2.44 (s, 3H), 3.31 (d, J = 13.8, 1H), 3.36 (d, J = 13.8, 1H), 4.38 (dd, J = 7.9, J = 4.8, 1H), 5.45 (d, J = 9.8, 1H), 6.54 (d, J = 9.8, 1H), 7.33 (d, J = 8.4, 2H), 7.79 (d, J = 8.4, 2H); ^{13}C NMR ($CDCl_3$) δ 20.1, 20.2, 21.8, 27.0, 31.9, 35.0, 44.4, 48.3, 50.0, 52.7, 68.1, 111.7, 126.3, 127.5, 130.0, 139.6, 144.5; IR 1608; HRMS m/z calcd for $C_{19}H_{26}NO_4S_2^+$ $[M + H]^+$ 396.1298, found 396.1293.

2h *(98:2 Z/E, 153 mg, 96%, with 0.03 equiv of Et_3N). Data for chromatographically pure N-[(Z)-2-(4-methylphenylsulfonyl)-ethenyl]-1,8-naphthosultam.* White solid; mp 188−190 °C; R_f = 0.24 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3H), 6.65 (d, J = 8.6, 1H), 6.82 (d, J = 8.6, 1H), 7.17 (dd, J = 6.9, J = 1.1, 1H), 7.27 (d, J = 8.3, 2H), 7.59−7.68 (m, 2H), 7.77 (dd, J = 8.1, J = 7.2, 1H), 7.85 (d, J = 8.3, 2H), 7.97 (d, J = 7.2, 1H), 8.13 (d, J = 8.1, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 108.4, 120.2, 120.2, 120.6, 127.8, 128.1, 128.4, 129.5, 129.5, 130.0, 130.9, 131.8, 132.1, 135.7, 137.2, 145.3; IR 1615; HRMS m/z calcd for $C_{19}H_{16}NO_4S_2^+$ $[M + H]^+$ 386.0515, found 386.0526.

2i *(>99:1 Z/E, 103 mg, 90%, with 0.2 equiv of NaH), N-[(Z)-2-(4-methylphenylsulfonyl)ethenyl]saccharin.* White solid; mp 168−170 °C; R_f = 0.55 (hexanes:EtOAc, 1:1); ^{1}H NMR (DMSO-d_6) δ 2.41 (s, 3H), 6.91 (d, J = 8.4, 1H), 7.36 (d, J = 8.4, 1H), 7.48 (d, J = 8.3, 2H), 7.80 (d, J = 8.3, 2H), 8.08 (td, J = 7.5, J = 0.6, 1H), 8.14 (td, J = 7.6, J = 1.0, 1H), 8.23 (d, J = 7.5, 1H), 8.43 (d, J = 7.4, 1H); ^{13}C NMR (DMSO-d_6) δ 21.1, 122.0, 122.0, 125.9, 126.1, 127.9, 130.0, 135.1, 135.8, 136.4, 136.5, 136.6, 145.1, 156.4; IR 1753, 1618; HRMS (ESI+) m/z calcd for $C_{16}H_{14}NO_5S_2^+$ $[M + H]^+$ 364.0308, found 364.0314. Purification by column chromatography was not necessary (and it is not recommended, because of partial decomposition).

General Procedure for the Addition of Imides, Azinones, Nucleosides, and Sultams to Tosylacetylene, To Obtain 3. Tosylacetylene (1.2 equiv) and the corresponding substrate were dissolved in CH_3CN (0.1 M) under a N_2 atmosphere. DMAP was then added, and the reaction was stirred at 20 °C or 50 °C (see Table 3) until TLC analysis indicated complete disappearance of the Z isomer (usually 1 or 2 days). The solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2. The organic layer was washed with 0.5 M aqueous HCl and brine, dried over anhyd $MgSO_4$, filtered, and concentrated. Purification by flash column chromatography on silica gel afforded pure **3**.

3a *(>99:1 E/Z, 1.36 g, 90%), 1-N-[(E)-2-(4-methylphenylsulfonyl)-ethenyl]succinimide.* White solid; mp 192−194 °C; R_f = 0.51 (hexanes/EtOAc, 20:80); ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 2.83 (s, 4H), 7.33 (d, J = 8.2, 2H), 7.58 (d, J = 14.2, 1H), 7.78 (d, J = 14.2, 1H), 7.78 (d, J = 8.2, 2H); ^{13}C NMR ($CDCl_3$) δ 21.8, 27.9, 121.1, 127.8, 128.5, 130.1, 137.7, 144.7, 174.1; IR 1731, 1622; HRMS m/z calcd for $C_{13}H_{14}NO_4S^+$ $[M + H]^+$ 280.0638, found 280.0632.

3b *(>99:1 E/Z, 1.47 g, 98%), N-[(E)-2-(4-methylphenylsulfonyl)-ethenyl]phthalimide.* White solid; mp 186−187 °C; R_f = 0.77 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 7.34 (d, J = 8.2, 2H), 7.52 (d, J = 14.3, 1H), 7.79−7.85 (m, 4H), 7.92−7.98 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 21.8, 119.0, 124.6, 127.8, 128.8, 130.1, 131.3, 135.6, 138.2, 144.5, 165.1; IR 1796, 1723, 1622; HRMS m/z calcd for $C_{17}H_{14}NO_4S^+$ $[M + H]^+$ 328.0638, found 328.0635.

3c *(>99:1 E/Z, 93 mg, 80%), 5′-O-acetyl-3′-azido-3′-deoxy-3-[(E)-2-(4-methylphenylsulfonyl)ethenyl]thymidine.* White solid; mp 98−100 °C; R_f = 0.30 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$) δ 1.94 (s, 3H), 2.12 (s, 3H), 2.34−2.39 (m, 1H), 2.42 (s, 3H), 2.46−2.57 (m, 1H), 4.06−4.09 (m, 1H), 4.18−4.22 (m, 1H), 4.32 (dd, J = 12.4, J = 3.6, 1H), 4.38 (dd, J = 12.4, J = 4.4, 1H), 6.05 (t, J = 6.1, 1H), 7.31 (m, 3H), 7.71 (d, J = 14.3, 1H), 7.78 (d, J = 8.0, 2H), 8.37 (d, J = 14.3, 1H); ^{13}C NMR ($CDCl_3$) δ 13.5, 20.9, 21.7, 37.9, 60.4, 63.2, 82.3, 87.0, 110.1, 123.3, 127.8, 130.0, 131.8, 134.2, 138.1, 144.5, 149.1, 161.6, 170.3; IR 2109, 1739, 1718, 1651; HRMS m/z calcd for $C_{21}H_{24}N_5O_7S^+$ $[M + H]^+$ 490.1391, found 490.1387.

3d *(>99:1 E/Z, 83 mg, 96%), N-[(E)-2-(4-methylphenylsulfonyl)-ethenyl]-2-pyridone.* White solid; mp 195−196 °C; R_f = 0.63 (CH_2Cl_2/MeOH, 98:2); ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 6.23 (br t, J = 6.8, 1H), 6.58 (br d, J = 9.1, 1H), 7.06 (d, J = 14.1, 1H), 7.28−7.37 (m, 4H), 7.82 (d, J = 8.3, 2H), 8.22 (d, J = 14.1, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 108.0, 120.1, 122.9, 127.9, 130.2, 133.0, 137.3, 137.8, 140.0, 144.8, 161.3; IR 1682, 1625; HRMS m/z calcd for $C_{14}H_{14}NO_3S^+$ $[M + H]^+$ 276.0689, found 276.0690.

3e *(>99:1 E/Z, 86 mg, 84%), 1-[(E)-2-(4-methylphenylsulfonyl)-ethenyl]-2-quinoxalinone.* White solid; mp 168−170 °C; R_f = 0.66 (CH_2Cl_2/EtOAc, 1:1); ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 7.36 (d, J = 8.2, 2H), 7.47 (ddd, J = 8.1, J = 7.2, J = 1.3, 1H), 7.59 (dd, J = 8.6, J = 1.4, 1H), 7.65 (ddd, J = 8.6, J = 7.2, J = 1.6, 1H), 7.84 (d, J = 8.4, 2H), 7.88 (d, J = 13.7, 1H), 8.07 (d, J = 13.7, 1H), 8.21 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 114.4, 125.9, 127.2, 127.9, 130.3, 130.7, 131.3, 131.4, 131.8, 133.4, 137.4, 145.0, 150.3, 154.0; IR 1681, 1612; HRMS m/z calcd for $C_{17}H_{15}N_2O_3S^+$ $[M + H]^+$ 327.0798, found 327.0802.

3f *(>99:1 E/Z, 52 mg, 90%), 2′,3′,5′-tri-O-acetyl-1-[(E)-2-(4-methylphenylsulfonyl)ethenyl]inosine.* White solid; mp 108−109 °C; R_f = 0.51 (CH_2Cl_2/MeOH, 95:5); ^{1}H NMR ($CDCl_3$) δ 2.09 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 2.44 (s, 3H), 4.35 (dd, J = 12.3, J = 4.6, 1H), 4.39−4.47 (m, 2H), 5.54 (t, J = 5.2, 1H), 5.81 (t, J = 5.4, 1H), 6.08 (d, J = 5.2, 1H), 7.36 (d, J = 8.2, 2H), 7.42 (d, J = 14.1, 1H), 7.82 (d, J = 8.2, 2H), 7.95 (s, 1H), 8.10 (s, 1H), 8.14 (d, J = 14.1, 1H); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.7, 20.9, 21.8, 63.0, 70.6, 73.6, 80.6, 86.5, 124.5, 127.9, 128.9, 130.3, 132.6, 136.2, 138.5, 145.9, 147.5, 147.6, 155.3, 169.4, 169.7, 170.4; IR 1748, 1712; HRMS m/z calcd for $C_{25}H_{27}N_4O_{10}S^+$ $[M + H]^+$ 575.1442, found 575.1447.

3g *(>99:1 E/Z, 580 mg, 82%), (S)-N-[(E)-2-(4-methylphenylsulfonyl)ethenyl]-2,10-camphorsultam.* White solid; mp 97−98 °C; R_f = 0.68 (CH_2Cl_2/MeOH, 99.5:0.5); ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 3H), 1.02 (s, 3H), 1.31 (t, J = 8.3, 1H), 1.43 (t, J = 9.1, 1H), 1.81 (dd, J = 12.9, J = 7.9, 1H), 1.90−1.95 (m, 3H), 2.07−2.15 (m, 1H), 2.41 (s, 3H), 3.31 (d, J = 13.9, 1H), 3.36 (d, J = 13.8, 1H), 3.48 (dd, J = 7.8, J = 4.8, 1H), 5.70 (d, J = 13.6, 1H), 7.30 (d, J = 8.2, 2H), 7.51 (d, J = 13.6, 1H), 7.74 (d, J = 8.2, 2H); ^{13}C NMR ($CDCl_3$) δ 20.0, 20.4, 21.7, 26.8, 32.3, 35.9, 44.7, 48.1, 50.3, 50.7, 64.5, 110.7, 127.4, 130.0, 134.8, 139.0, 144.0; IR 1609; HRMS m/z calcd for $C_{19}H_{26}NO_4S_2^+$ $[M + H]^+$ 396.1298, found 396.1293.

3h *(>99:1 E/Z, 56 mg, 97%), N-[(E)-2-(4-methylphenylsulfonyl)-ethenyl]-1,8-naphthosultam.* White solid; mp 181−183 °C; R_f = 0.30 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 6.72 (d, J = 13.9, 1H), 7.18 (m, 1H), 7.35 (d, J = 8.4, 2H), 7.66−7.68 (m, 2H), 7.80−7.86 (m, 1H), 7.84 (d, J = 8.4, 2H), 7.90 (d, J = 13.9, 1H), 8.02 (d, J = 7.3, 1H), 8.18 (d, J = 8.4, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 21.8, 105.6, 112.5, 118.8, 120.5, 121.4, 127.6, 128.6, 128.9, 129.5, 130.1, 130.6, 131.0, 132.3, 132.5, 138.5, 144.4; IR 1622; HRMS m/z calcd for $C_{19}H_{16}NO_4S_2^+$ $[M + H]^+$ 386.0515, found 386.0525.

N-[(E)-2-(4-Methylphenylsulfonyl)ethenyl]saccharin, ***3i.*** A solution of DMAP (4 mg, 0.03 mmol) and **2i** (228 mg, 0.627 mmol) in CH_3CN (6.3 mL) was stirred overnight at rt. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (hexanes:EtOAc, 1:1) to afford **3i** (205 mg, 90%, >99:1 E/Z) as a White solid: mp 208−209 °C; R_f = 0.54 (hexanes/EtOAc, 1:1); ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 6.93 (d, J =

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14.3, 1H), 7.36 (d, J = 8.0, 2H), 7.83 (d, J = 8.0, 2H), 7.92−8.00 (m, 4H), 8.17 (d, J = 7.3, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 118.0, 121.6, 126.0, 126.5, 127.0, 127.9, 130.2, 135.4, 136.3, 137.3, 137.6, 144.9, 156.2; IR 1739, 1623; HRMS m/z calcd for $C_{16}H_{14}NO_5S_2^+$ $[M + H]^+$ 364.0308, found 364.0304.

General Procedure for the Preparation of 4. LiHMDS (1.5 equiv, 1.0 M in THF) was added dropwise to a solution of the substrate in THF (0.1 M) under a N_2 atmosphere at 0 °C. (*Z*)-1,2-Bis(phenylsulfonyl)ethene (1.5 equiv) was then slowly added, and the reaction was stirred until TLC analysis indicated complete consumption of the starting material (a few minutes). The reaction mixture was diluted with H_2O and extracted with EtOAc. The combined organic layers were washed with brine, dried over anhyd $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel.

***4a** (93:7 Z:E, 97 mg, 95%). Data for chromatographically pure 1-[(Z)-2-(phenylsulfonyl)ethenyl]succinimide, **4a**.* White solid; mp 118−120 °C; R_f = 0.48 (hexanes/EtOAc, 20:80); ^{1}H NMR ($CDCl_3$) δ 2.88 (s, 4H), 6.44 (d, J = 9.0, 1H), 6.58 (d, J = 9.0, 1H), 7.54−7.59 (m, 2H), 7.63−7.70 (m, 1H), 7.92−7.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 28.9, 126.6, 128.2, 129.4, 129.7, 134.3, 139.8, 174.5; IR 1730, 1637; HRMS (ESI+) m/z calcd for $C_{12}H_{12}NO_4S^+$ $[M + H]^+$ 266.0482, found 266.0486.

***4j** (94:6 Z/E, 155 mg, 95%). Data for chromatographically pure 1-[(Z)-2-(phenylsulfonyl)ethenyl]-2-pyrrolidinone.* White solid; mp 116−118 °C; R_f = 0.52 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$) δ 2.08−2.18 (m, 2H), 2.50 (t, J = 8.1, 2H), 4.22 (t, J = 7.3, 2H), 5.58 (d, J = 10.7, 1H), 7.19 (d, J = 10.7, 1H), 7.53−7.59 (m, 2H), 7.61−7.66 (m, 1H), 7.91−7.96 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.3, 29.9, 48.9, 108.2, 126.9, 129.3, 130.8, 133.3, 142.6, 175.8; IR 1721, 1603; HRMS (ESI+) m/z calcd for $C_{12}H_{14}NO_3S^+$ $[M + H]^+$: 252.0689, found: 252.0691.

***4k** (90:10 Z/E, 109 mg, 90%). Data for chromatographically pure 5-tert-butyldiphenylsilyloxymethyl-N-[(Z)-2-(phenylsulfonyl)-ethenyl]-2-pyrrolidinone.* White solid; mp 160−162 °C; R_f = 0.80 (CH_2Cl_2/EtOAc, 1:1); ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 9H), 2.09−2.33 (m, 2H), 2.45 (ddd, J = 17.9, J = 10.2, J = 2.1, 1H), 2.80 (dt, J = 17.9, J = 10.2, 1H), 3.58 (dd, J = 11.4, J = 1.9, 1H), 3.87 (dd, J = 11.4, J = 2.2, 1H), 5.09 (br d, J = 8.9, 1H), 5.40 (d, J = 10.8, 1H), 6.98 (d, J = 10.8, 1H), 7.31−7.36 (m, 2H), 7.37−7.47 (m, 6H), 7.48−7.52 (m, 3H), 7.54−7.57 (m, 2H), 7.72−7.76 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 19.1, 21.5, 26.9, 30.2, 59.8, 64.3, 109.3, 126.9, 127.8, 127.9, 129.2, 130.0, 130.0, 132.6, 132.9, 133.3, 135.7, 135.8, 141.9, 176.6; IR 1713, 1605; HRMS m/z calcd for $C_{29}H_{34}NO_4SSi^+$ $[M + H]^+$: 520.1972, found 520.1976.

***4l** (94:6 Z/E, 139 mg, 90%). Data for chromatographically pure (S)-4-benzyl-3-[(Z)-2-(phenylsulfonyl)ethenyl]-1,3-oxazolidin-2-one.* White solid; mp 119−121 °C; R_f = 0.76 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$) δ 2.64 (dd, J = 13.3, J = 10.3, 1H), 3.58 (dd, J = 13.3, J = 3.4, 1H), 4.21−4.23 (m, 2H), 5.50 (m, 1H), 5.61 (d, J = 10.8, 1H), 7.02 (d, J = 10.8, 1H), 7.23−7.27 (m, 1H), 7.29−7.37 (m, 4H), 7.52−7.58 (m, 2H), 7.60−7.66 (m, 1H), 7.94−7.98 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 36.4, 57.4, 66.2, 109.3, 127.1, 127.3, 128.9, 129.4, 129.8, 130.0, 133.7, 135.0, 141.6, 155.6; IR 1762, 1617; HRMS m/z calcd for $C_{18}H_{18}NO_4S^+$ $[M + H]^+$: 344.0951, found 344.0954.

General Procedure for the Preparation of 5. NaH (1.1 equiv) and 15-crown-5 (1.5 equiv) were added to a solution of the substrate in THF (0.1 M) under a N_2 atmosphere at 0 °C. (*E*)-1,2-Bis(phenylsulfonyl)ethene (which is rather insoluble in most solvents, 1.3 equiv) was then added in portions, and the reaction was stirred at rt until TLC analysis indicated complete consumption of the starting material (around 4 h). The reaction mixture was diluted with H_2O and extracted with CH_2Cl_2. The combined organic fractions were washed with brine, dried over anhyd $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel.

***5a** (>99:1 E/Z, 99 mg, 97%), 1-[(E)-2-(phenylsulfonyl)ethenyl]-succinimide, **5a**.* White solid; mp 186−187 °C; R_f = 0.32 (hexanes/EtOAc, 20:80); ^{1}H NMR ($CDCl_3$) δ 2.83 (s, 4H), 7.52−7.57 (m, 2H), 7.59 (d, J = 14.2, 1H), 7.60−7.65 (m, 1H), 7.82 (d, J = 14.2, 1H), 7.90−7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 27.9, 121.0, 127.8, 128.9, 129.5, 133.7, 140.7, 173.9; IR 1715, 1621, 1365, 1132; HRMS (ESI+) m/z calcd for $C_{12}H_{12}NO_4S$+ $[M + H]^+$ 266.0482, found 266.0485.

***5j** (>99:1 E/Z, 570 mg, 91%), 1-[(E)-2-(phenylsulfonyl)ethenyl]-2-pyrrolidinone.* White solid; mp 143−145 °C; R_f = 0.39 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$) δ 2.09−2.17 (m, 2H), 2.52 (t, J = 8.2, 2H), 3.47 (t, J = 7.3, 2H), 5.72 (d, J = 13.7, 1H), 7.46−7.52 (m, 2H), 7.54−7.59 (m, 1H), 7.84−7.87 (m, 2H), 8.05 (d, J = 13.7, 1H); ^{13}C NMR ($CDCl_3$) δ 17.5, 30.8, 45.2, 110.2, 127.2, 129.3, 133.1, 136.2, 142.0, 174.4; IR 1727, 1610; HRMS (ESI+) m/z calcd for $C_{12}H_{14}NO_3S^+$ $[M + H]^+$: 252.0689, found: 252.0693.

***5k** (>99:1 E/Z, 133 mg, 90%), 5-tert-butyldiphenylsilyloxymethyl-N-[(E)-2-(phenylsulfonyl)ethenyl]-2-pyrrolidinone.* White solid; mp 164−165 °C; R_f = 0.73 (CH_2Cl_2/EtOAc, 1:1); ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 9H), 2.16−2.22 (m, 2H), 2.41−2.50 (m, 1H), 2.74 (dt, J = 17.9, J = 10.3, 1H), 3.57 (dd, J = 10.9, J = 2.9, 1H), 3.76 (dd, J = 10.9, J = 4.2, 1H), 3.84−3.91 (m, 1H), 5.75 (d, J = 14.0, 1H), 7.33−7.39 (m, 4H), 7.40−7.45 (m, 2H), 7.47−7.52 (m, 4H), 7.53−7.59 (m, 3H), 7.78−7.81 (m, 2H), 7.99 (d, J = 14.0, 1H); ^{13}C NMR ($CDCl_3$) δ 19.2, 22.0, 26.8, 30.5, 58.5, 62.8, 110.4, 127.2, 128.1, 128.1, 129.2, 129.9, 130.2, 130.3, 132.1, 132.7, 132.9, 135.5, 135.5, 135.6, 142.2, 175.1; IR 1730, 1612; HRMS m/z calcd for $C_{29}H_{34}NO_4SSi^+$ $[M + H]^+$: 520.1972, found 520.1976.

***5l** (>99:1 E/Z, 170 mg, 96%), (S)-4-benzyl-3-[(E)-2-(phenylsulfonyl)ethenyl]-1,3-oxazolidin-2-one.* White solid; mp 162−163 °C; R_f = 0.63 (CH_2Cl_2/MeOH, 99:1); ^{1}H NMR ($CDCl_3$) δ 2.83 (dd, J = 14.0, J = 7.9, 1H), 3.09 (dd, J = 14.0, J = 4.1, 1H), 4.23−4.30 (m, 2H), 4.31−4.36 (m, 1H), 5.93 (d, J = 13.9, 1H), 7.10 (d, J = 8.1, 2H), 7.20−7.30 (m, 3H), 7.52−7.57 (m, 2H), 7.59−7.64 (m, 1H), 7.82 (d, J = 13.9, 1H), 7.89 (d, J = 8.1, 2H); ^{13}C NMR ($CDCl_3$) δ 37.2, 55.7, 67.4, 110.7, 127.4, 127.9, 129.3, 129.3, 129.4, 133.3, 134.1, 136.6, 141.8, 154.2; IR 1749, 1614; HRMS m/z calcd for $C_{18}H_{18}NO_4S^+$ $[M + H]^+$: 344.0951, found: 344.0954.

Removal of the Tsv Group. Method A. A suspension of dodecanethiol (1.5 equiv) and NaH (3.0 equiv) in CH_3CN was added to a solution of the protected substrate in anhyd CH_3CN (0.1 M). The resulting mixture was stirred at the temperature shown in Table 4 until TLC indicated complete consumption of the starting material. The reaction was quenched with water, neutralized with 0.5 M aqueous HCl, and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel.

Removal of the Tsv Group. Method B. A suspension of sodium 1-dodecanethiolate (1.2 equiv) in CH_3CN was added to a solution of the protected substrate in anhyd CH_3CN (0.1 M). TLC indicated complete consumption of the starting material after stirring at 0 °C or rt for a few minutes (see Table 4). The reaction was quenched with water, neutralized with 0.5 M aqueous HCl, and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel.

Removal of the Tsv and Bsv Groups. Method C. Pyrrolidine (2.0 equiv) was added to a solution of the protected substrate in anhyd CH_3CN (0.1 M), and the mixture was stirred at rt or 55 °C (see Table 4) until TLC indicated complete consumption of the starting material. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel.

Removal of the Tsv and Bsv Groups. Method D. Pyrrolidine (2.0 equiv) and NaH (0.3 equiv) were added to a solution of the protected substrate in anhyd CH_3CN (0.1 M). The mixture was stirred at 55 °C until TLC indicated complete consumption of the starting material. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(9) We attribute this fact to the higher tendency of DABCO to be involved in the concomitant formation of a tosylacetylene dimer (Ts−C≡C−CH═CH−Ts, δ 6.72 and 6.93, ^3J = 15.4 Hz, which we have confirmed by blank experiments with Ts−C≡CH and catalytic amounts of DABCO) and subsequent additions, including polymerization, which also makes the separation of the desired product more difficult. There is only one precedent of a similar dimerization: (a) Sardari, S.; Khalaj, V.; Khomeini, M. M.; Azerang, P. U.S. Patent 2013 8,569,361B1. By contrast, dimerizations of propynoate esters are much better known: (b) Ramachandran, P. V.; Rudd, M. T.; Reddy, M. V. R. *Tetrahedron Lett.* **2005**, *46*, 2547−2549 and references cited therein. (c) Reference 2 (and ref 10 cited therein).

(10) (*Z*)-Bis(phenylsulfonyl)ethene (purchased from TCI Europe) was nearly a 98:2 *Z*/*E* mixture by ^{1}H NMR. Isomer *E* (also purchased from TCI Europe) was >99% pure. There are precedents of stereospecific reactions of these two reagents with nucleophiles. See: (a) Knapp, S.; Levorse, A. T. *J. Org. Chem.* **1988**, *53*, 4006−4014. (5-iodomethyl-2-pyrrolidinone). For reaction with 1,3-oxazolidine-2-thiones or a derivative of 1,3-oxazine-2-thione, see: (b) Girniene, J.; Tardy, S.; Tatibouët, A.; Sačkus, A.; Rollin, P. *Tetrahedron Lett.* **2004**, *45*, 6443−6446. (c) Tardy, S.; Tatibouët, A.; Rollin, P.; Dujardin, G. *Synlett.* **2006**, *45*, 1425−1427. (d) Leconte, N.; Silva, S.; Tatibouët, A.; Rauter, A. P.; Rollin, P. *Synlett* **2006**, 301−305.

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(14) For example, heating **2b** with 0.5 equiv of DMAP, in CH_3CN at 50 °C for 48 h, gave a 10:90 mixture of **2b** and **3b**.

(15) Spectral data for **6**: ^{1}H NMR (DMSO-d_6, 400 MHz) δ 2.41 (s, 3H), 3.29 (s, 6H), 7.16 (d, J = 7.4, 2H), 7.50 (d, J = 7.9, 2H), 7.54−7.59 (m, 3H), 7.60−7.66 (m, 1H), 7.75 (d, J = 13.8, 1H), 7.83 (d, J = 7.9, 2H), 8.15 (d, J = 13.8, 1H), 8.54 (d, J = 7.5, 2H); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 21.1, 40.6, 108.1, 119.1, 119.9, 122.4, 127.3, 130.2, 130.9, 131.5, 134.9, 137.3, 139.4, 140.9, 144.8, 145.3, 156.7, 167.8; HRMS (ESI+) m/z calcd for $C_{16}H_{19}N_2O_2S^+$ $[M]^+$ 303.1162, found: 303.1165.

(16) Tertiary amines and the DMAP/tosylacetylene adducts are not basic enough to significantly deprotonate lactam CONH groups, so the conjugate addition reactions do not progress. When the lactam anions are generated with strong bases and tosylacetylene is added, proton exchanges occur to give the starting lactams (no reaction) and tosylacetylide, Ts−C≡C$^-$, which polymerizes (also see ref 9).

(17) We carried out one experiment of this type. We treated the sodium salt of butyrolactam (**1j**) with **6** (*E*-DMAP$^+$CH═CHTs Sacc$^-$; see Scheme 3) in CH_3CN at 25 °C. The reaction was complete in less than 30 min. Compound **3j** was isolated in ≥90% yield.

(18) The N,S-acetals (thiohemiaminals) were detected by ^{1}H NMR of the crude reaction mixtures. Characteristic signals (for the thiohemiaminal derived from **3b** and dodecanethiol, $CDCl_3$, 400 MHz): δ 3.56 (dd, J = 14.9, J = 2.6, 1H), 4.67 (dd, J = 14.9, J = 11.7, 1H), 5.71 (dd, J = 11.7, J = 2.6, 1H).

(19) Isolation and characterization of the aminal (addition product) from **4j** and pyrrolidine as follows. Pyrrolidine (67 μL, 0.81 mmol) was added to a solution of **4j** (51 mg, 0.20 mmol) in CH_3CN (2 mL).

After the reaction was stirred for 4.5 h at rt, TLC indicated that the starting material had disappeared to give a less polar product. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH 99:1) to give the corresponding aminal, **7** (61 mg, 0.19 mmol, 92%): oil; R_f = 0.20 (CH_2Cl_2/MeOH 99:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.59−1.71 (m, 4H), 1.71−1.81 (m, 1H), 1.82−1.92 (m, 1H), 2.19−2.29 (m, 2H), 2.39−2.46 (m, 2H), 2.48−2.54 (m, 2H), 3.27−3.36 (m, 2H), 3.48 (dd, J = 14.8, J = 3.3, 1H), 3.66 (dd, J = 14.8, J = 9.9, 1H), 4.89 (dd, J = 9.9, J = 3.3, 1H), 7.52−7.58 (m, 2H), 7.61−7.67 (m, 1H), 7.89−7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 18.4, 23.5, 31.4, 44.5, 49.8, 55.6, 65.4, 128.4, 129.3, 134.0, 139.2, 176.0; HRMS (ESI+) m/z calcd for $C_{16}H_{23}N_2O_3S^+$ $[M + H]^+$ 323.1424, found: 323.1464.

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